ROLE OF HEPARIN IN THE MANAGEMENT OF BURNS

By

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ABSTRACT

BACKGROUND

Burn trauma represents a major cause of morbidity and mortality, as well as a significant drain on limited health resources. 40 patients with burns ranging from 05 to 40% TBSA were treated with topical Heparin. The burn trauma ranged from superficial to 2nd degree burns. They were all evaluated for 1 week in hospital and were followed up for a month.

OBJECTIVES

Heparin application or administration is a much better treatment modality in patients presenting to the emergency room within 72hrs of burn trauma as Heparin prevents Burn extension, promotes faster healing via neovascularization and reduces the days of hospitalization when compared to conventional treatment with Silver Sulphadiazine.

METHODS

All body parts which have sustained burn trauma are exposed adequately and cleansed with normal saline solution before topical application of Heparanised Sodium Solution to the same area drop by drop via 30 gauge needle. All blebs were injected with the same solution and not de-roofed. This was done for 7 days post presenting in Hospital (Day1 TID, Day 2 BD, and Day 3-7 OD dressing with Heparin application). All patients received antibiotics twice daily and analgesics were administered once daily and SOS.

RESULTS

Application of Heparin topically to burns patients significantly reduced the days of hospitalization, amount of analgesics and antibiotics required; Heparin also promoted neovascularization and reduced tissue edema.

CONCLUSIONS

Heparin application should be made the preferred modality of treatment for patients presenting to the emergency room with more than 10% to 40% TBSA as it is better accepted by patients and reduces the post burn complications significantly.

Key Words: Burns, Heparin, Topical Heparin

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INTRODUCTION

"*Heat cannot be separated from Fire or beauty from the eternal"*

A million years ago, in the desert sands of Kalahari, South Africa, sitting in a cave, the species known as *Homo Erectus*, our ancestors, discovered fire. They controlled the use of fire in such ways that they were able to keep their bodies warm in the nights, scare away animals that posed a threat to them or their kind and even kill their prey and cook them to have a meal which was easily digestible to them using the same fire. This was one of the first big discoveries that man would forever be proud of. Ever since then, Man has toyed with fire in all the ways he deemed possible. But this came with a price! The day he was at the receiving end of the wrath of Fire, he set forth on a journey to find remedies to curb the nasty effects of this Marvel….he is yet to reach his destination.

The recognition and treatment of burns can be seen in numerous cave paintings dated more than 3500 years old. As on today, the Fraternity of Surgeons have come a long way from treating burn wounds with resin and honey as professed by the Egyptians to primary tangential excision and skin grafting with recombinant skin tissue. The understanding of the pathophysiology of burn trauma by the German and the Greek doctors allowed the treatment of burns and prevention of contractures. With the technological advancements of the modern world and the concept oriented multidisciplinary approach to the problem, Surgeons are able to resuscitate and rehabilitate the patient to reduce the morbidity and mortality associated with burns and help the patient recover to a functionally and socially acceptable state.

Heparin is an anticoagulant in its natural form. The non-anticoagulant effects of Heparin form the rationale for using heparin to treat burn trauma. Heparin is a

multifaceted compound with anti-inflammatory, anti-histaminic, anti-allergenic, anti-serotonin, and anti-proteolytic, Neoangiogenic and anti-metastatic agent. The use of heparin provides adequate pain relief, reduces tissue edema, prevents burn contractures, and promotes faster healing and revascularisation. Re-epithelisation is faster with regeneration of granulation tissue.

The Morbidity and mortality associated with burn trauma is dreaded. Our hospital being the only fully equipped and dedicated centre capable of handling burn cases (in an area spanning 80kms) and treating the patients, who come from a financially challenged and educationally backward class, we have taken up the task to explore the lesser known but equally beneficial effects of heparin in order treat burn trauma. The challenge is to reduce the amount of days of hospitalization, provide treatment at an affordable cost and improve the quality of life of the patient and help in a speedy recovery and a faster return to their work as able society members.

AIM

The primary aim of this dissertation is to study the beneficial effects of the multifaceted compound – Heparin in the treatment of burn wounds and its sequelae in terms of:

a. Pain Relief
b. Prevention of Burn Extension
c. Prevention of Inflammation
d. Reduction of Tissue Edema
e. Neoangiogenesis &
f. Revascularisation
g. Prevention of Contractures

OBJECTIVES

The objectives of this study are to compare the effectiveness and efficiency of Heparin with the conventional treatment methods in the treatment of burn wounds with regards to:

a. Limited usage of Analgesics
b. Reduction in Burn area extension
c. Decrease in tissue edema
d. Reduction in topical sepsis
e. Increase in rate of revascularisation
f. Reduction in days of hospitalisation
g. Early Mobilization and Return to Work

REVIEW OF LITERATURE

The recognition of burn wounds and subsequent quest in finding a cure for the same dates back to early civilization where man used anything and everything he could get his hands on to soothe the pain. The Egyptians in 1500BC documented the use of a concoction made of resin and honey for the treatment of burns. In 600BC, the Chinese, known for their profound admiration of herbs, made use of tinctures and extracts of tea leaves, for their medicinal values, to treat burns[1].

In the same year, a sea and a nation across, a scholar, a person with profound medical knowledge and a genius level intellect had already classified the burn wounds according to their causes and degree of skin and tissue involvement. He was treating the wounds with herbal oils and tangentially excising the wound area when and where needed and raising flaps and fixing skin grafts to treat the burn wound area without a shred of doubt about the good prognosis. He is known today, throughout the world, as the Father of Plastic Surgery. His name is Sushrutha! This surgeon from India is known for his immense contribution to the world of surgery through his Sushrutha Samhitha[2].

In 15th century AD, the French Surgeon, Ambroise Paré effectively treated burn wounds with onions and he was probably one of the first to describe a procedure for early burn wound excision. In 1607, a German Surgeon, Guilhelmus Fabricius Hildanus, published a book, De Combustionibus, in which he described the pathophysiology of burn wounds and made unique contributions to the treatment of burn contractures [3].

The treatment of burns was started with topical application of a variety of substances and this was second only to the number of physicians and surgeons treating the same.

From the use of honey, herbal oils, vinegar, wine and cold water to the usage of a concoction made of pig fat and resin, oak barks, hot soot, lime water and paraffin, anything that eased the suffering was used to treat burns[1]. The Scholars and Philosophers, Physicians and Surgeons alike contributed to the same.

From the likes of Hippocrates & Rhases, an Arabian physician, to the men of modern era, namely, Galen, Edward Kentish & Guillaume Dupuytren, all these men have contributed immensely in understanding the pathophysiology, treatment and management aspect of Burn trauma[4.]

Truman G. Blocker Jr may have been the first to demonstrate the value of a multidisciplinary team approach to a burn disaster during the 'Texas City Disaster' which killed nearly 560 people and injured more than 3000 people in the year 1947 [5].

As early as 1947, researchers had recognized that prompt eschar removal and immediate wound closure could improve outcome in burn injuries. Application of this approach to large burns had not been practical before the 1970's because of an associated high rate of infection, bleeding complications and requirement of large quantity of blood. Many burn units adopted the excision technique in which a single tangential slice was intended to remove the superficial layer of 2nd degree injuries [6, 7].

In the near future new standards of care potentially available for burn treatment would be liposomal gene transfer, the use of artificial skin substrates, such as dermal matrices with epidermal components, amniotic wound coverage devices and dermal component matrices [8-11].

Burn wound is a wound in which there is coagulative necrosis of proteins in dermal and epidermal parts of tissues or tissue injury from thermal heat or cold application or from the absorption of physical energy of chemical contact[1].

Burns and Burn trauma can be best understood under the following headings:

I. Definition

II. Classification

- According to the Causative Agent
- According to the Type of Burn trauma

III. Depth of Burn Trauma

- First Degree
- Second Degree
- Third Degree
- Fourth Degree

IV. Estimation of Burn trauma in TBSA

- The Wallace "Rule of Nine"
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❖ DEFINITION:

A burn may be defined as dissolution in tissue continuity consequent on thermal damage. It is a wound in which there is coagulative necrosis of proteins in tissues or injury to tissues from thermal heat application or exposure to extreme cold or due to the absorption of physical energy by conduction via contact with chemicals or radiation.

❖ CLASSIFICATION:

Burn trauma is classified according to

Table 1: Causative Agent

TYPE	CAUSE
Flame	Damage due to superheated or oxidised air
Scald	Damage due to contact with hot liquids
Conduction via Contact	Damage due to contact with hot/cold surfaces
Chemical	Damage due to contact with acids/alkalis
Electrical	Damage due to contact with electric current

Table 2: Type of Burn Trauma

TYPES OF BURNS	LEVEL OF INVOLVEMENT IN TISSUES
Scald	Superficial to Partial thickness skin loss
Flame	Patches of Full thickness skin loss
Fat burns	Full thickness skin loss
Electrical Burns	Full thickness skin loss with deeper extension
Frostbite	Local Vasospasm, Crust formation
Ionizing Radiation	Tissue necrosis due to exposure to excessive cGy
Chemical Burns	Tissue Necrosis with Systemic effects

❖ DEPTH OF BURN TRAUMA: [1,12,13]

Thermal injury or burn trauma can involve various layers of epidermis, dermis, subcutaneous tissue, fat and even viscera. They are classified according to the degree of involvement of tissues:

i. First Degree Burns

ii. Second Degree Burns

iii. Third Degree Burns

iv. Fourth Degree Burns

- **First Degree Burns** are superficial burns involving only the epidermis and are erythematous and present with minimal oedema. They typically heal within five to seven days and topical antimicrobial therapy is not really indicated. (Ex: Sunburn, Flame Burn)
- **Second Degree Burns** are injuries that involve epidermis & a part of dermis and hence can be sub-classified as superficial second degree and deep second degree. **Superficial second degree** burns are pinkish-red, moist, and erythematous and blanch on touching. They heal within twelve to fourteen days and usually do not leave a scar. These are best treated with topical antimicrobial agents and paraffin or greasy gauze application. **Deep second degree** burns involve the entire epidermis and extend into the reticular portion of dermis, present typically as a dry wound with mottled pinkish-white appearance with loss of sensation to touch but remain tender to pressure or needle pricks. These typically need about 18-21 days to heal with adequate protection from infection. If healing is delayed beyond 3 weeks (upto 8 weeks), then application of various skin substitutes or split thickness skin grafting is a more viable option. Both Superficial and Deep Second degree burns involve the hair follicles and sweat glands, the difference being that the former heals with regeneration of the lost tissues and the latter heals with minimal scarring post re-granulation.

- **Third Degree Burns** involve the entirety of epidermis and dermis and are hence referred to as full thickness burns. These present as leathery (usually brown-black), completely mottled, insensitive to touch and pressure. They heal by scarring as no epidermal and dermal layers remain for regeneration, hence wound edges act as sample tissues from which regeneration starts. Excision of burn area and split thickness or complete thickness skin grafting yields productive results in these patients. Healing period is variable.
- **Fourth Degree Burns** involve the viscera beneath all protective layers of subcutaneous tissue. Commonly muscles and long bones are involved. Management of these depend upon the area and the extent of involvement. (Ex: Electric Burns)

Table 3: Degree of burns

Old Nomenclature	Revised Nomenclature	Depth of Involvement	Presenting Features
First Degree	Superficial	Only Epidermis	Pink, Erythematous, mild pain, no blisters
Second Degree	Superficial Partial thickness	Epidermis and Papillary Dermis	Pinkish-Red, painful, Oedematous with blisters
Second Degree	Deep Partial Thickness	Involvement of Reticular Dermis	Appear white and pale, painless
Third & Fourth Degree	Full thickness	Dermis and underlying deeper tissues	Brown-black leathery eschar, insensitive

❖ Estimation of Burn Trauma: [14]

Estimating a burn size with regards to total body surface area (TBSA) is essential in calculating the amount of fluid required to resuscitate a patient. The following have been used as a standard in most centres to calculate the TBSA involved:

- Lund & Browder Chart
- The Wallace “Rule of Nine”
- The “Rule of Palms”

- **Lund and Browder Chart:** This was first described to calculate the TBSA of burn trauma in children as their head is of a greater proportion of body mass in comparison to their body, which differentiates them from adult TBSA. [12-14]

Table 4: Lund and Browder chart.

	A					
	1	**1 to 4**	**5 to 9**	**10 to 14**	**15**	**Adult**
Area Burned	**Percentage of Total Body Surface**					
Head	19	17	13	11	9	7
Neck	2	2	2	2	2	3
Anterior Trunk	13	13	13	13	13	13
Posterior Trunk	13	13	13	13	13	13
Left Buttock	2.5	2.5	2.5	2.5	2.5	2.5
Right Buttock	2.5	2.5	2.5	2.5	2.5	2.5
Right Upper Arm	4	4	4	4	4	4
Left Upper Arm	4	4	4	4	4	4
Right Lower Arm	3	3	3	3	3	3
Left Lower Arm	3	3	3	3	3	3
Right Hand	2.5	2.5	2.5	2.5	2.5	2.5
Left Hand	2.5	2.5	2.5	2.5	2.5	2.5
Right Thigh	5.5	6.5	8	8.5	9	9.5
Left Thigh	5.5	6.5	8	8.5	9	9.5
Right Lower Leg	5	5	5.5	6	6.5	7
Left Lower Leg	5	5	5.5	6	6.5	7
Right Foot	3.5	3.5	3.5	3.5	3.5	3.5
Left Foot	3.5	3.5	3.5	3.5	3.5	3.5

- **The Wallace "Rule of Nines" Chart**: This chart is used world over as a routine to calculate the TBSA of burn trauma in adults. This chart is also useful in calculating the amount of fluid that should be used in resuscitation.

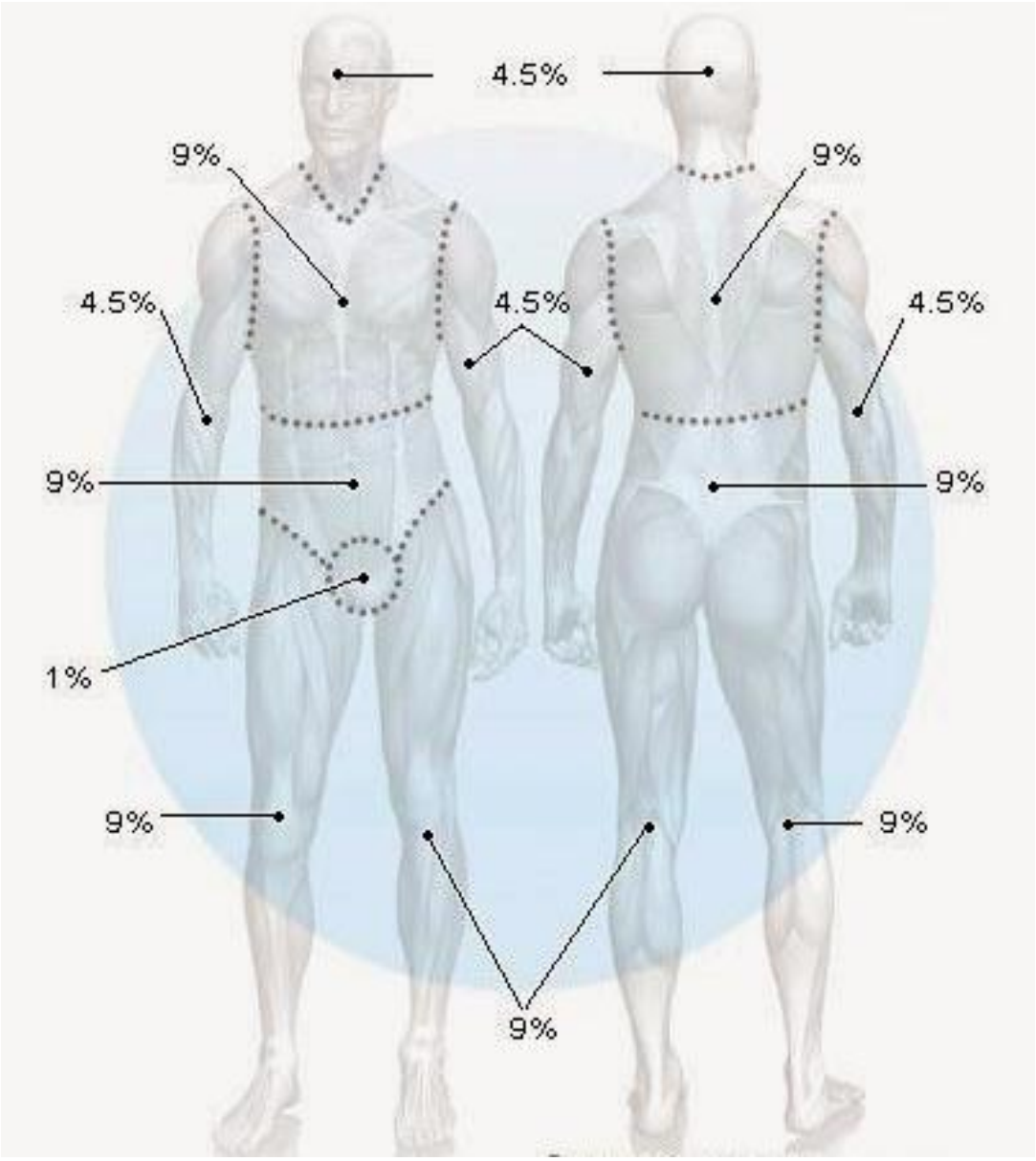


Figure 1: Wallace's Rule of Nine

- **The "Rule of Palms":** This technique is useful in calculating percentage of burn trauma in small and minimal burns and in burns involving patches with intact healthy skin in between.

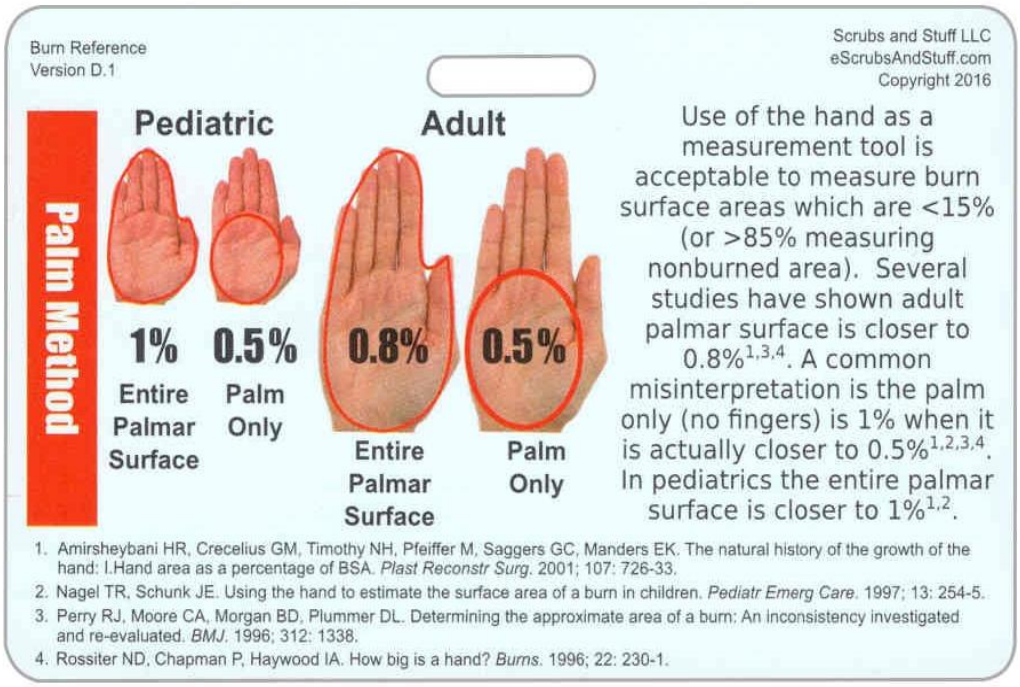


Figure 2: Rule of Palms

❖ Categorization of Burn Severity: [14]

The categorization of the severity of burn trauma includes the following factors:

i. The Site, Extent and Depth of Burn Injury

ii. Age of the Patient

iii. Aetiology of the Burn Trauma

iv. Presence or Absence of Inhalational Injury

v. Associated Co-morbid conditions/ Pre-existing Illness

The above parameters were used to establish and set guidelines to categorize and classify the severity of burn trauma by The American Burn Association. They have defined the categories into 3 classes:

I. Minor Burn Injury:
II. Moderate Burn Injury
III. Major Burn Injury

- **Minor Burn Injury:** These include the following
    a. Burn trauma involving less than 15% TBSA in adults or less than 10% in extremes of age (i.e. children and elderly)
    b. Full thickness burns involving less than 2% of TBSA but do not present as a serious threat of functional or cosmetic risk to the eyes, ears, face, hands, feet and perineum.

    These are burn injuries that are managed on outpatient basis and effectively treated conservatively.
- **Moderate Burn Injury:** These include the following
    a. Partial thickness burns of 15-25% of TBSA in adults or 10-20% of TBSA in children or elderly
    b. Full thickness burns involving 2-10% of TBSA but do not present as a serious threat of functional or cosmetic risk to the eyes, ears, face, hands, feet and perineum. This category excludes high-voltage electrical injury.
    c. All burns complicated by inhalational injury or other trauma and burn trauma sustained by high risk patients.

    Patients with moderate burn injury should be hospitalised for initial management and treatment but need not be in a burn centre.

- **Major Burn Injury:** These include the following

    a. Partial thickness burns involving more than 25% of TBSA in adults and more than 20% of TBSA in children less than 10 years.

    b. Adults older than 50 years, having full thickness burns more than 10% TBSA; burns involving eyes, ears, face, hands, feet or perineum that result in functional or cosmetic impairment.

    c. Burns caused by caustic chemical agents.

    d. High-voltage Electrical injury, burns complicated by inhalational injury or major trauma.

    e. Burns sustained by high risk patients.

    These patients are best managed at a dedicated burn centre with professionals who expertise in treating burn patients in acute care, resuscitation and rehabilitation.

- **Burn Center Referral Criteria:** [16]

The American Burn Association (ABA) has identified the following injuries as those requiring referral to a burn center after the patient has been assessed and stabilised primarily in a hospital:

i. Partial thickness burns and full thickness burns amounting to more than 10% TBSA in patients under 10 years or over 50 years of age.

ii. Partial thickness burns and full thickness burns amounting to more than 20% TBSA in other age groups.

iii. Partial thickness burns or full thickness burns involving face, hands, feet, genitalia, perineum and any major joints.

iv. Full thickness burns amounting to more than 5% TBSA in any age group.

v. Electrical burns including lightning injury.

vi. Chemical Burns.

vii. Inhalational burns with burn injury.

viii. Circumferential burns with burn injury.

ix. Any burn injury with concomitant trauma in which the burn injury poses a greatest risk of morbidity and mortality. However, if the trauma poses a greater immediate risk, the patient should be initially treated until stable and then to be transferred to a burn centre.

x. Burn injury in patients with pre-existing medical disorders that could complicate management, prolong recovery period or affect mortality.

xi. Burn injury in children admitted in hospitals without qualified personnel or equipment for paediatric care.

xii. Burn injury in patients requiring social, emotional and or long term rehabilitative support including cases involving suspected child abuse.

❖ <u>Pathophysiologic Response:</u>

These are categorised into two types:

➢ Local Response:

The skin provides an effective barrier to the transfer of energy to the deeper tissues, but however even after the initiating focus is removed; the response of local tissues can cause an injury to the deeper tissue layers.

The three zones [13] of a burn wound are three dimensional and were described by Jackson in 1947 as follows:

i. **Zone of Coagulation** – This occurs at the point of maximum damage. There is irreversible tissue loss due to coagulation of the constituent proteins in this zone.

ii. **Zone of Stasis** – The surrounding zone of stasis is characterised by decreased tissue perfusion. This zone is an area in which the tissue injury can be reversed if adequate resuscitation is given at the right time. The main aim of burn trauma resuscitation is to increase tissue perfusion here and prevent any damage becoming irreversible. Additional insults such as prolonged hypotension, infection or oedema can convert this zone into an area of complete tissue loss.

iii. **Zone of Hyperaemia** - In this outermost zone, tissue perfusion is increased. The tissue in this zone usually recovers unless there is severe sepsis or prolonged period of hypo perfusion.

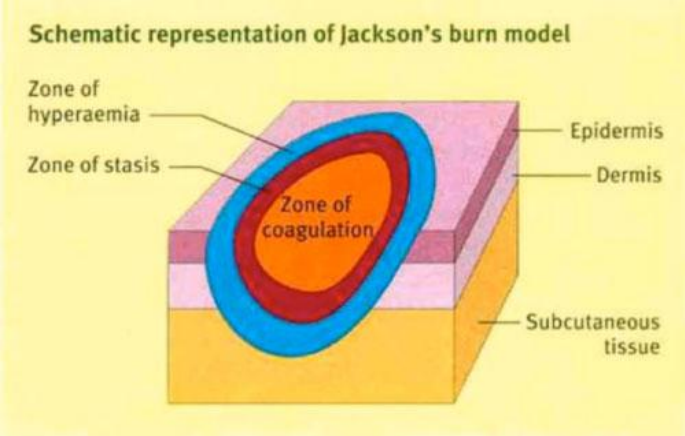


Figure 3: Jackson Burn Model

Burns are followed by the development of an area of hyperalgesia (and/or allodynia) around the lesion, which is known as the area of Primary hyperalgesia. Surrounding this area, a zone of Secondary hyperalgesia appears in the intact skin and gradually increases in diameter with time. Hyperalgesia indicates a greater sensitivity to pain caused by the reduction in the pain threshold and an increase in the intensity of responses to the supraliminal noxious stimuli. In comparison, Allodynia is a painful sensation induced by normally non painful, supraliminal noxious stimuli.

In the area of Secondary hyperalgesia, there are symptoms only for mechanical stimuli and not for heat. In the normal skin, heat resulting in painful sensation by nociceptors, carries a risk of tissue damage; but the hyperthermia used in post-heat shock tolerance is too mild to induce any specific tissue injury. This mild painful stimulus can result in the induction of descending anti-nociceptive mechanisms, especially in the adjacent burnt area. Some of these inhibitory mechanisms can modify peripheral tissue inflammation as mentioned above[17].

- Systemic Response:

  A wide variety of inflammatory mediators involved in burn trauma are responsible for most of the systemic effects. Burn trauma initiates systemic inflammatory reactions producing toxins and oxygen radicals which finally lead to per oxidation. The relationship between the amount of oxidative metabolism and natural scavengers of the free radicals determines the outcome of local and distant tissue damage and further organ failure in burn injuries [18, 19].

  The various systemic effects of burn injury can be discussed under following headings:

  i. Effects on cardiovascular system
  ii. Effects on respiratory system
  iii. Metabolic response to burn trauma

  The effects on cardiovascular system: The changes in the heart and blood vessels begin almost immediately after burn trauma. The extent of these changes depends primarily on the size of the burn trauma and to a lesser extent on the depth of the burn. Immediate cardiovascular response to thermal injury is a reduction in cardiac output along with an elevation in

peripheral vascular resistance. In the absence of a cardiac pathology, ventricular ejection fraction and velocity of the myocardial fibre shortening are actually increased during thermal injury. Severe burn trauma results in significant hypovolaemic shock and substantial tissue trauma, both of which cause the formation and release of many local and systemic mediators which further continue the pathological cascade [18].

The effects on respiratory system: The changes in pulmonary functions after the burn trauma are similar to those seen in other forms of traumatic injuries. Respiratory minute ventilation usually increases as soon as the burn trauma occurs. After resuscitation, the respiratory rate and tidal volume progressively increase which in turn increase the minute ventilation. Pulmonary vascular resistance also increases after burn trauma, which may be a manifestation of the release of vasoactive amines and other mediators and may provide a protective effect during the fluid resuscitation by reducing the pulmonary capillary hydrostatic pressure thus lowering susceptibility to pulmonary edema[17].

Metabolic response to burn trauma:

a) Hypermetabolic and Neuroendocrine response
b) Effects on Gastrointestinal system
c) Effects on Renal system
d) Effects on Immune system

Hypermetabolic and Neuroendocrine response: The primary mediators of hypermetabolic response following burn trauma greater than 40% are Catecholamines and Corticosteroids. They raise upto fifty fold and last upto

nine months post burn trauma in the body. Burn patients have increased resting energy expenditure, increased cardiac workload, increased myocardial oxygen consumption, marked tachycardia, severe lipolysis, liver dysfunction, severe muscle catabolism, increased protein degradation, insulin resistance and growth retardation [20].

Effects on Gastrointestinal System: Burn trauma causes the degradation of muscle protein and release of massive amounts of amino acids from muscle. Increased cortisol levels and decreased growth hormone and insulin, result in increased proteolysis of muscle and release of amino acids. The basal energy expenditure id increased three fold above normal and the calorie requirement rises three and a half times normal requirement per day. Early and aggressive nutritional support via enteral route is important in preventing bacterial translocation from the gut and systemic sepsis[22].

Effects on Renal system: In acute phase of burn injury, renal blood flow and glomerular filtration rate (GFR) as measured by increase in creatinine clearance, shows impairment in tubular function. As the phase of burn trauma progresses, decrease in the blood volume and cardiac output cause a decrease in renal blood flow and glomerular filtration rate, which if not corrected with adequate fluid resuscitation results in oliguria which progresses to acute renal failure (ARF)[23]. This is associated with high mortality rates.

Effects on Immune system: It has been implied that the elevated production of PGE_2 & Nitrous oxide by macrophages can suppress T-cell activity and impaired T-cell function may be the end point in the development of burn trauma induced immunosuppression[25].

❖ Treatment of Burns:

Pre Hospital

Before undergoing any specific treatment burned patients must be removed from the source of injury and the burning process stopped. While removing the patient from the source of injury, care must be taken to ensure that the rescuer does not become another victim .Some amount of inhalation injury is always present and 100% oxygen should be given by facemask. Burnt clothing is extinguished and removed as soon as possible to prevent further injury. Room-temperature water can be poured on the wound within 15 minutes of injury to decrease the depth of the wound, but any subsequent measures to cool the wound are avoided to prevent hypothermia during resuscitation.

Initial Assessment

As with any trauma patient, the initial assessment of a patient with burn trauma is divided into a primary and a secondary survey[12]. In the primary survey, immediate life threatening conditions are quickly identified and treated. In the secondary survey, a more thorough head-to-toe evaluation of the patient is undertaken.

Primary Survey: The initial management of a patient with burn trauma is similar to that of any trauma patient. A thorough primary survey is performed with the following in mind:

A. Airway with Cervical Spine control

B. Breathing and Ventilation

C. Circulation

D. Disability

E. Exposure

F. Fluid Resuscitation

Airway with Cervical Spine Control:

An assessment must be made as to whether the airway is compromised or is at risk of compromise. The cervical spine should be protected unless it is definitely not injured. Inhalation of hot gases will result in a burn above the vocal cords and this area will become oedematous as time progresses, especially after fluid resuscitation has begun which means that an airway that is patent on arrival at hospital may occlude after admission especially in small children. Acute upper airway obstruction occurs in approximately one-fifth to one-third of hospitalized burn victims with inhalation injury and is a major problem because of the possibility of rapid progression from mild pharyngeal oedema to complete upper airway obstruction with asphyxia[15, 18]

Breathing and Ventilation:

There are several ways that a burn trauma can compromise respiration. Mechanical restriction of breathing can occur in deep dermal burns or full thickness circumferential burns of the chest. These can limit chest movements during inspiration and prevent adequate ventilation: usually requires escharotomy and/or debridement. A blast injury or an explosion

can cause lung trauma and contusion over lung surface, cause alveolar trauma and progress to ARDS. These can complicate ventilation and can cause tension pneumothorax if penetrating injury is present. It is advisable to initiate 100% oxygen to all patients who present with burn trauma, through a non-rebreathing mask.

Circulation:

Intravenous access should be established with two or three large bore cannula, preferably placed through unburnt tissue on presentation in patients with more than 20% burns. Any deep or full thickness circumferential extremity burn can act as a tourniquet, especially once oedema develops after fluid resuscitation. If there is any suspicion of decreased perfusion due to circumferential burn, the tissue must be released with escharotomy.

Disability:

All patients should be assessed for level of consciousness using Glasgow coma scale as they may be have clouding of their consciousness because of hypoxia or hypovolaemia.

Exposure:

The patient should be examined by removing all clothing to get an accurate estimate of total burn area and to check for any concomitant injuries. Burn patients are susceptible to hypothermia. Hence, after estimating the burn area, the clothing (preferably hospital sterilised gown) should be used to cover the patient and provide adequate warmth as soon as possible.

Fluid resuscitation:

The fluid resuscitation regimen should be determined and begun. This is based on the estimation of the burn area. A urinary catheter is mandatory in all adults with burns covering > 20% of total body surface area to monitor urine output and in patients with abdominal burns to check the abdominal compartment pressures. In children urine output can be monitored by weighing nappies, provided the injury is < 20% of total body area. In children the interosseous route can be used for fluid administration if intravenous access cannot be obtained, but should be replaced by intravenous lines as soon as possible[27]. The ultimate goal of resuscitation is to maintain adequate tissue perfusion and to therefore preserve organ function. Delays in resuscitation must be minimized as delays result in poorer outcomes. The adequate resuscitation of a burned patient depends on establishment and maintenance of reliable intravenous access. The traditional method of assessing the adequacy of resuscitation has been based on the observations of blood pressure, heart rate and urine output, and fluids are titrated as to maintain a urine output of 0.5-1ml/min or 30-50ml/hr. (refer table 5)

Table 5: Fluid resuscitation Formulas:

Formula	Fluid in First 24 Hours	Crystalloids in	Titration
Parkland	RL at 4 mL/kg per percentage burn	20-60% estimated plasma volume	Titrated to urinary output of 30 mL/h
Evans	NS at 1 mL/kg per percentage burn, 2000 mL D5W*, and colloid at 1 mL/kg per percentage burn	50% of first 24-hour volume plus 2000 mL D5W	50% of first 24-hour volume
Slater	RL at 2 L/24 h plus fresh frozen plasma at 75 mL/kg/24 h		
Brooke	RL at 1.5 mL/kg per percentage burn, colloid at 0.5 mL/kg per percentage burn, and 2000 mL D5W	50% of first 24-hour volume plus 2000 mL D5W	50% of first 24-hour volume
Modified Brooke	RL at 2 mL/kg per percentage burn		
Metro Health (Cleveland)	RL solution with 50 mEq sodium bicarbonate per liter at 4 mL/kg per percentage burn	Half NS titrated to urine Output	1 U fresh frozen plasma for each liter of half NS used + D5W as needed for Hypoglycemia
Monafo hypertonic Demling	250 mEq/L saline titrated to urine output at 30 mL/h, dextran 40 in NS at 2 mL/kg/h for 8 hours, RL titrated to urine output at 30 mL/h, and fresh frozen plasma 0.5 mL/h for 18 hours beginning 8 hours post burn	One-third NS titrated to urine output	
Ideal formula	2-4ml RL/kg/%burns	Maintain urine output 0.5- 1 ml/kg	50% of the dose given in 24 hrs
Augmented electrolyte solution	5%dextrose saline + 20 mEq of Sodium Bicarbonate 3ml/kg/%burns	Maintain urine output 0.5-1 ml/kg	50% of the dose given in 24 hrs

Gastrointestinal dysmotility, ranging from a moderate delay in gastric emptying to marked gastro paresis, has been described in critically ill patients with conditions such as burns. To combat any regurgitation and to decompress the stomach in patients with intestinal ileus, a nasogastric tube is inserted in all patients with major burns. Decompression of the stomach is necessary because the apprehensive patient will swallow considerable amounts of air and distend the stomach [28].

Secondary Survey:

At the end of primary survey and the start of emergency management, a secondary survey should be performed:

- Elicit a thorough Medical history
- Thorough Head-to-toe examination
- Estimate Burn Size and Depth with diagrammatic representation
- Tetanus Prophylaxis
- Antibiotics, analgesics and sedatives
- Psychiatric counselling

- **Burn Wound Management:**

DRESSINGS:

In the past, many burn surgeons dressed wounds twice daily until complete healing occurred or surgical intervention was required for wound closure. This practice has changed to daily dressing changes, resulting in a significant decrease in costs, nursing time, and pain.

Tannic acid spray was used by Davidson in 1925. To reduced pain and produce a cleaner wound bed. Gentamycin sulfate was briefly utilized as 0.1% topical cream burn dressing, intended for anti-pseudomonas coverage of invasive burn wounds but now discontinued due to its ototoxictiy and nephrotoxicity.

Silver sulfadiazine a sulfa derivative topical antibacterial used as a topical burn cream on second- and third-degree burns has broad-spectrum antibacterial activity and is associated with relatively few complications. The efficacy of silver sulfadiazine is thought to result from its slow and steady reactions with serum and other sodium chloride containing body fluids, which permits the slow and sustained delivery of silver ions into the wound environment.

Escharotomy:

Severely burned extremities should be elevated, reverse trendelenberg position and range of motion exercises for the limbs performed every 15-30 minutes as tolerated by the patient to minimize tissue edema and tissue pressures. Indications for emergency escharotomy are the presence of a circumferential eschar with any one of the following features:

- Impending or established vascular compromise of the extremities or digits
- Impending or established respiratory compromise [28]

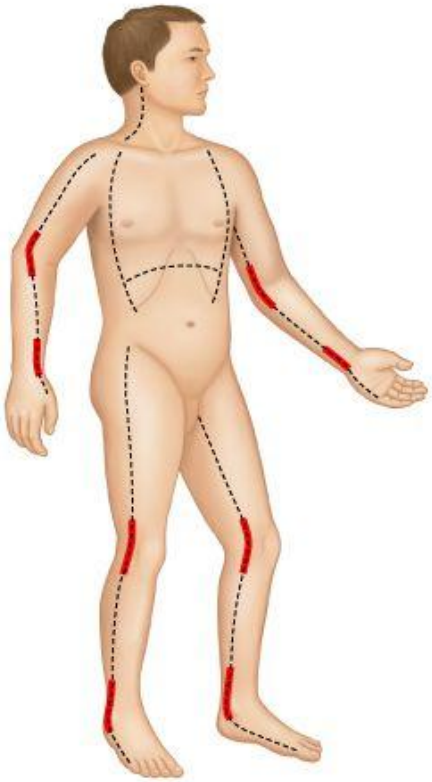


Figure 4: Escharotomy Incisions

Skin Grafting in Burns: [29-31]

Skin grafting in burns is not a new concept. Reverdin applied small grafts to an old burn ulcer as early as 1869.In 1886, a German surgeon named Carl Thiersch described the technique of skin grafting using a straight razor to excise long thin strips of skin containing some dermis and applying them to a freshly debrided granulation tissue bed. Since then various types of grafts like the pinch graft, sandwich graft etc have been used. Both allografts and xenografts have been used in burn treatment. Initial grafts were obtained free hand with long, thin bladed knives. Finochietto developed an improved knife for controlling the depth of skin harvest in 1920 followed by multiple improvements in surgical burn knives. Braithwaite, Watson, Goullian and Humby are names still associated with knives used to harvest skin and remove burned tissues today.

As the art and science of skin grafting developed it became clear early on that allograft skin, while a good temporary burn covering, was not a long-term solution to treating burns. As grafting of larger burned areas was undertaken, methods to provide broader coverage of the excised bed were needed, when the concept of "meshing" the skin graft to allow it to stretch for greater coverage was introduced. Lanz, a German surgeon made a hand held device for meshing and this was further improved by the hand cranked double roller graft mesher developed by Tanner and Vandeput. Current graft meshers function in a similar fashion. Today electrical dermatomes like that of Brown, Padgets, etc can take graft from any site in the body and mesh it.

The timing of surgical intervention and grafting in burns had previously been an area of spirited debate. Tangential excision refers to the shaving of multiple thin parallel layers of the burn until healthy tissue. The efficacy of this technique was confirmed in a study by Heimbach. The technique of tissue cultures has been further refined and it is now possible to grow large sheets of the patient's epidermal cells in tissue cultures which can then be transferred to the prepared burn wound to provide autologous epidermal coverage. Effective techniques using artificial skin substitutes have also been tried in burn treatment.

The ideal skin replacement product is one that is readily available off the shelf, is dependable, easy to use, and infection resistant, has a low profile of side effects, demonstrates an acceptable appearance, is reasonably priced and restores both the dermal and epidermal layers of the skin to its original state. Skin substitutes are often categorised as either temporary or permanent and are also thought of as products that provide temporary wound coverage of wound closure.

Temporary skin substitutes, as a group, include a collection of varied, topically applied agents that are thought to offer more than a simple protective covering to a healing burn. Such skin substitutes include products that have inherent healing properties of their own or have added biologically active substances, presumably able to advance wound healing. The term “skin substitute” entered the burn literature in the 1980s when Burke *et al* developed a skin substitute “Integra”.

Integra was approved by the United States FDA for use in the treatment of burns in 1996. It is a bilayered skin substitute composed of an outer layer of silicone, covering a bioengineered collagen matrix. The product is marketed as a “dermal regeneration template” that allows the in growth of fibroblasts, vascular tissues and cells in a more organized fashion. While the bovine collagen in the dermal template is ultimately replaced by the patient’s collagen and cell in growth, the reformed “neodermis” has architecture that more closely resembles normal dermis than that of simple scar tissue. The outer semi permeable silicone membrane functions as a protective barrier while revascularization and remodelling occur, much like normal epidermis. After maturation of the framework, this neodermis is covered by thin sheets of the patient’s auto graft skin.

Dermal replacement products offer many advantages. When healing is complete, the amount of scar tissue formation in the wound is markedly decreased. This results in a measured improvement in elasticity and flexibility of the healed burn. Scar contracture is lessened and leads to a reduction in the number of scar contracture procedures and plastic surgical reconstructions required long term. Dermal replacement has therefore been a major advancement in the treatment of burns.

Heparin

Heparin is a naturally occurring anticoagulant produced by basophils and mast cells[32]. In 1916, McLean, a second-year medical student at Johns Hopkins University, while working under the guidance of Howell investigating pro-coagulant preparations, isolated a fat-soluble phosphatide anti-coagulant in canine liver tissue. It was Howell in 1918 who coined the term heparin (from hepar, Greek for liver) for this type of fat-soluble anticoagulant in 1918. Marcum's paper on "The origin of the dispute over the discovery of heparin" gives a full discussion of heparin's discovery and subsequent history. Heparin, also known as unfractionated heparin, is a highly-sulphated glycosaminoglycan, which is widely used as an injectable anticoagulant and has the highest negative charge density of any known biological molecule. Heparin is given parenterally because it is not absorbed from the gut, due to its high negative charge and large size. Heparin can be injected intravenously or subcutaneously (under the skin); intramuscular injections (into muscle) are avoided because of the potential for forming hematomas. Antidote for heparin toxicity or reversal of heparin's effects is Protamine Sulphate found in certain fish's semen.

Heparin is generally used for anticoagulation for the following conditions:

- Acute Coronary Syndrome (ex: NSTEMI)
- Atrial Fibrillation
- Deep vein Thrombosis
- Pulmonary embolism
- Cardiopulmonary bypass for Heart surgery

Heparin and Burns:

Various studies have proven that heparin provides adequate analgesia when used in the treatment of burns [34-40] .The work of Ramakrishna [33] showed that heparin when

used in the management of burns had anti inflammatory properties. The work of Saliba[36] proved that heparin was added in the management of burns, not only did it reduce pain, but, also limited the inflammation caused revascularization of ischemic tissue and enhanced tissue granulation.

Studies were performed in patients with burn trauma using large doses of intestinal source of aqueous heparinised sodium solution (USP) for injection, administered both topically and parenterally early post burn during the initial burn ischemic acidosis period, and then only topically in diminishing doses into final healing, found large doses of intestinal or lung source heparin significantly reduced myocardial ischemic injury, and intestinal source heparin was significantly more cellular protective than lung heparin. Heparin therapy consistently relieved pain, reduced inflammation, and limited cellular-destruction, was neoangiogenic, regulated tissue restoration, shortened and facilitated healing and resulted in smooth healing. Patients were more alert, physically active, cooperative, and able to eat and help in their care. There was significant reduction in need for escharotomies and fasciotomies and skin grafting [34]

Heparin is an antagonist to histamine, bradykinin and prostaglandin E_1 combined with platelets inhibited complement C_1 esterase; protective against toxic oxygen metabolites and it also bound to TNF. Pulmonary problems were notably absent when aerosolized heparin was used to treat burned humans. . Alternating aerosolized inhalations of 5000 I.U. heparin or 3 ml of a aerosolized 20% solution of the mucolytic n-acetylcystene, resulted in a significant decrease in the rate of re-intubation for progressive pulmonary failure, the incidence of atelectasis and the mortality [41].

MATERIAL AND METHODS

A total of 40 patients admitted in BLDEU's Shri B M Patil Medical College, Hospital and Research Centre, Vijayapur in Surgery wards and Burns ward during October 2015 to May 2017 were included in our study with a sample size of 20 patients in each group. Patients with age less than 50 years and with a total burn surface area of less than 40% were included in this study after obtaining clearance from the ethical committee and the patient and/or the relative's consent to go ahead with the above mentioned study. They were divided into two groups- Heparin Group (H) of 20 patients and the Control Group (C) of 20 patients. The Heparin group received topical heparin therapy from the day of admission and in the Control group, the patients were given conventional treatment i.e. with topical silver sulphadiazine cream and paraffin gauze dressing.

INCLUSION CRITERIA

These are the Patients:

- Having TBSA Burns of >5% to <40%
- Presenting to the hospital within 72hrs of Burn Trauma
- Who are more than 15 years and less than 50 years of age
- Having Superficial to 2nd degree Burns

EXCLUSION CRITERIA

These are the Patients:

- Who are hypersensitive to Heparin
- Who are actively Bleeding
- With very Low Platelet Counts or altered APTT/PT/INR

- With a personal or familial History of Bleeding disorders
- With a recent or active Duodenal or gastric Ulcer
- With a history of Heparin Induced Thrombocytopenia in the past
- With full thickness burns
- With infected wounds or wounds with areas of necrosis

The treatment meted out to these patients included administration of antibiotics and analgesics systemically along with proton pump inhibitors and sufficient intravenous fluids as per the required dosage calculated for each and every patient (Parkland's Formula). Water baths were given on a daily basis to all patients (both groups). The only difference was that one group was treated with Topical Heparin application and the other group was regularly dressed with silver based antimicrobial cream and paraffin gauze. Debridement was kept to the bare minimal in the control group. There was no skin releasing incisions taken or escharotomies performed during the course of the treatment. Skin grafting was not done for any patient.

Injection Unfractioned Heparin 25000IU/5ml i.e. 5000IU/ml was used in the topical application for every patient. The source being from porcine intestinal mucosa, recommended for use in human burn injuries and trauma, was used.

Initial Evaluation and Procedures:

The initial evaluation and procedures on admission to the Burn Unit were the same in all 40 patients. Urgent life-threatening respiratory and/or cardiac emergency were managed first. Vital signs were measured and charted. Intravenous catheter was inserted, blood for laboratory tests was withdrawn, and intravenous resuscitation fluids were started. The burn size in total body surface area (TBSA) and the severity of burned areas was determined by clinical assessment and by the various formulas

for the same. Patients with burns of lower limbs and genital area were catheterized and urine output was measured. A personal and family medical history was recorded. A physical examination was performed. Bathing or cleaning of contaminated burns was done. Fluid intake, output volumes and laboratory tests were charted and evaluated. The initial routine laboratory tests done were: a Complete Blood Count and Urine analysis; Blood Urea and Creatinine; Blood grouping; Bleeding and clotting profile were done. A Chest X-ray was done as and when required. All patients were given prophylactic injection of Tetanus Toxoid.

Analgesics were administered as and when required i.e. parenteral injections of Tramadol were used for the first three to five days and later oral NSAIDs were allowed. Analgesics were omitted from treatment chart unless and until indicated.

Antibiotics were typically given after the culture sensitivity test was done. A 3rd generation Cephalosporin (Ceftriaxone) and an Imidazole group (Metronidazole) of antibiotics were started intravenously on presentation to casualty. Daily water baths were given to patients in both groups.

Method of Preparation of Heparin Solution for Topical Use:

Unfractioned Heparin which is available in 5ml vials of 5000IU/ml strength was used. One vial was mixed with 100ml of Normal Saline or Five vials with 500ml Normal Saline was stirred to make Heparinised Sodium Solution fit for topical application on Burn Wounds. The dose of heparin required for topical application was calculated to be 100,000IU/15% burn surface area (BSA) per day in 3-4 divided doses. The medication was applied to the burnt surface drop by drop with a 20 mL syringe and a 30 gauge needle (Insulin Syringe), until the pain was relieved, repeated for 2-4 times with 10 minute intervals until blanching occurred. Beginning on the 2nd day, heparin was applied twice a day, for two days and was used in a diminishing quantity for 1

week. Burn area was observed for neovascularisation and signs of healing i.e. appearance of granulation tissue and epithelisation.

Burn area was checked for extension every day. Blisters were treated using the #30 gauge needle on a 10ml syringe filled with the heparinised solution, the needle was inserted into the blister and a small hole was made to allow the burn fluid to drain. Then slowly heparin solution began to run out. It created a rinsing action. It was repeated for over three times and the cycle was repeated two to three times at 5 to 10 minute intervals. Blisters were never de-roofed.

Clotting Times were repeated during the course of heparin treatment to monitor the dose of Heparin. APTT and INR were also done. This was done to look into the systemic absorption of topically applied and its effects on the bleeding profile of the patient.

Heparin treatment was started as soon as the patient was received in the Casualty or Burns Ward after the initial assessment and resuscitation was complete and was continued till post burn day 7. The side effects of heparin and/or alteration of the bleeding profile were monitored and if present were a definitive indication for stopping heparin, and the effects would be reversed with Protamine sulphate 1 ml diluted with 9 ml of distilled water over ten minutes. The burn wounds were analyzed for early healing; better relief of pain; decreased wound infection; and shorter hospital stay.

STATISTICAL EVALUATION

The study data was statistically analyzed to evaluate the differences in Control Group and Heparin Group. Student‘t’ test, Chi square test, Paired ‘t’ test and Fishers exact test were used to assess the statistically significant values. Values of $p<0.01$ or less were considered to be statistically significant, designated by‘s’, those statistically not significant, by ‘NS’.

Sample Size

Prospective, interventional study

- With Anticipated Mean difference of total Healing days between two study groups (Conventional Treatment vs Topical Heparin Treatment) as 7 days with >5% to <40% Burns and anticipated Standard Deviation (SD) as 6.2, the minimum sample size per group is 20 patients in each group with 90% Power and 5% Level of significance.
- Calculated sample size is 20 in each group.
- In this study 40 cases will be studied, in each group 20 cases will be allocated alternatively.

Total Sample Size: 40

Control: 20

Case Study: 20

RESULTS & ANALYSIS

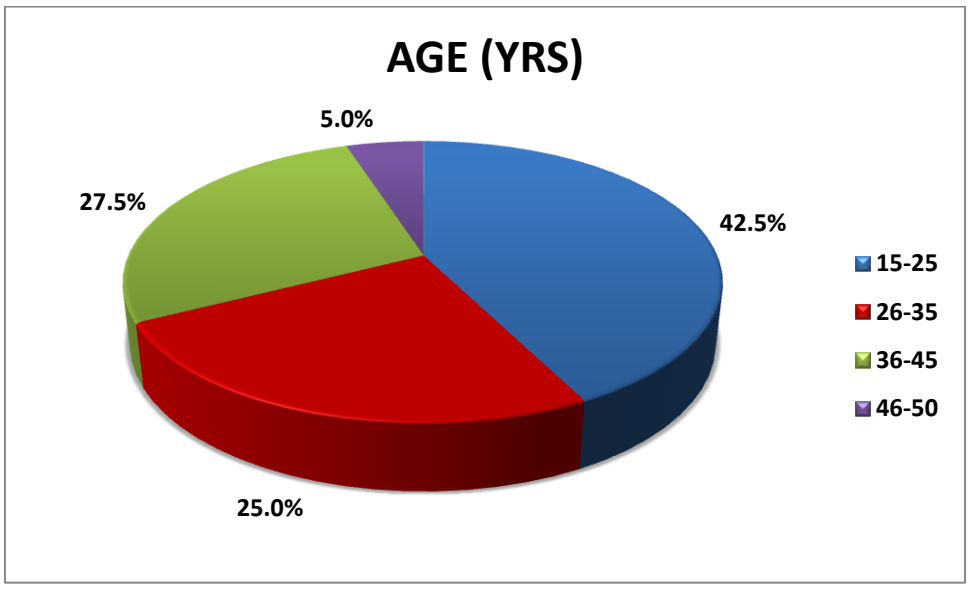
A total of 40 patients were included in the study and were randomly divided into two groups, 20 patients in Heparin (H) Group and 20 patients in Control (C) Group.

TABLE 6: DISTRIBUTION OF CASES ACCORDING TO AGE

Age	Group H	Group C	Total	%
15-25	9	8	17	42.5
26-35	5	5	10	25
36-45	4	7	11	27.5
46-50	2	0	2	5

	Minimum	Maximum	Mean	SD
AGE (YRS)	15	50	30.05	10.7

Graph 1: DISTRIBUTION OF CASES ACCORDING TO AGE

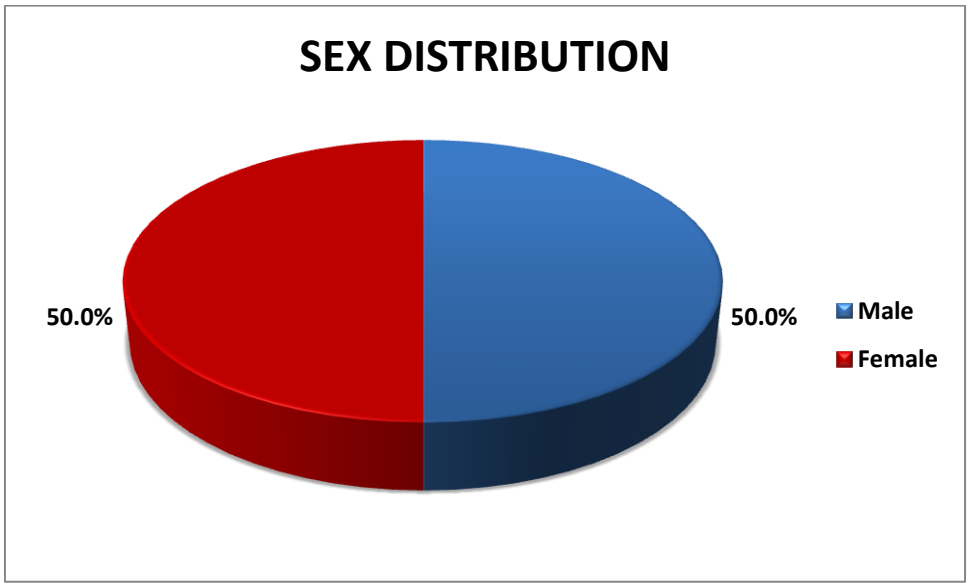


Maximum no of patients belonged to the reproductive and economically productive age group (15-35years=65.5%)

Table 7: Sex Distribution

Sex	Group H	Group C	Total	%
Males	9	11	20	50
Females	11	9	20	50
Total	20	20	40	100

Graph 2: DISTRIBUTION OF CASES ACCORDING TO SEX

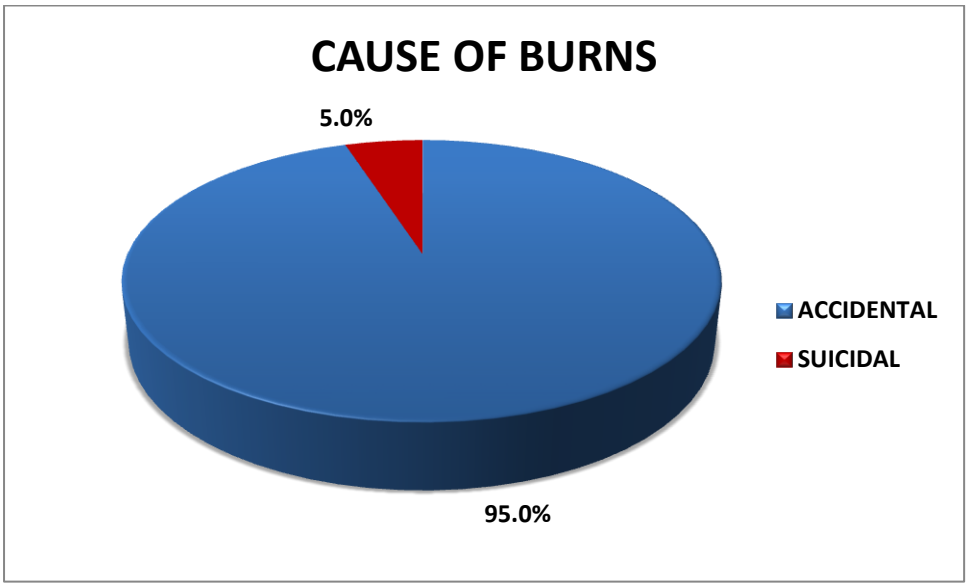


The Heparin Group had 9 male (45%) and 11 female (55%) patients as compared to the control group which had 11 male (55%) and 9 (45%) female patients. However, when combined the study and control group had equal number of male to female patient's ratio (20:20).

Table 8: Cause of Burns

Cause	Total	%
Accidental	38	95
Suicidal	2	5
Homicidal	0	0
Total	40	100

GRAPH 3: DISTRIBUTION OF CASES ACCORDING TO CAUSE OF BURNS



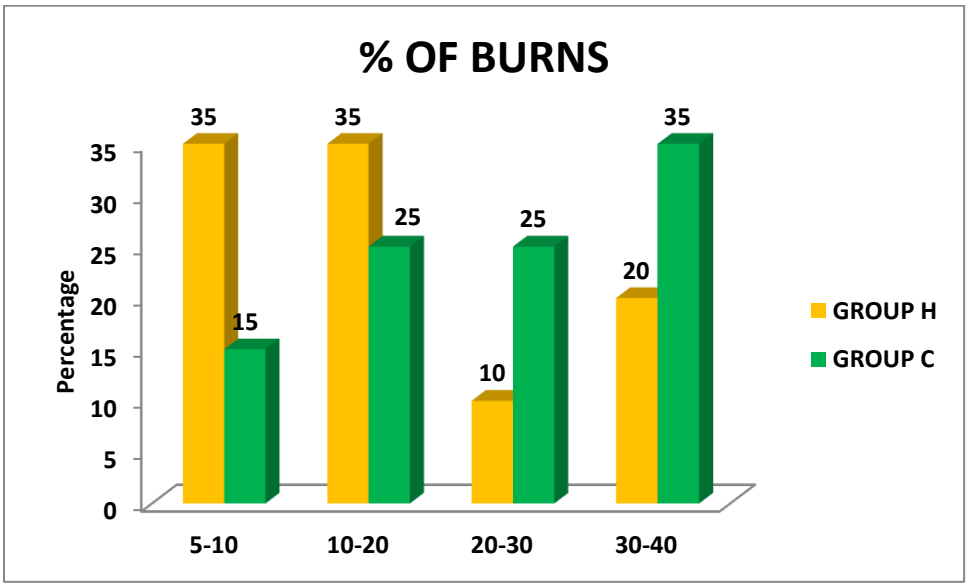
The study conducted showed that almost all patients barring two individuals had accidental burn trauma (95%) and the two individuals sustained burn injury due to a suicidal intent (5%). There were no homicidal burn injuries encountered. Both male and female patients were sufferers in accidental type of burn trauma but when it came to suicidal intent, both patients were female.

Percentage of Burns:

TABLE 9: DISTRIBUTION OF CASES ACCORDING TO % OF BURNS BETWEEN STUDY GROUPS

% OF BURNS	GROUP H		GROUP C		p value
	N	%	N	%	
5-10	7	35.0	3	15.0	0.257
11-20	7	35.0	5	25.0	
21-30	2	10.0	5	25.0	
31-40	4	20.0	7	35.0	
Total	20	100.0	20	100.0	

GRAPH 4: DISTRIBUTION OF CASES ACCORDING TO % OF BURNS BETWEEN STUDY GROUPS



The maximum number of patients who sustained thermal injuries was from 11-20% (12 patients) and 31-40% (11 patients). Together they make up 57.5%. The least number were in 21-30% (7 patients).

Age of the Patients:

GRAPH 5: DISTRIBUTION OF CASES ACCORDING TO AGE BETWEEN STUDY GROUPS

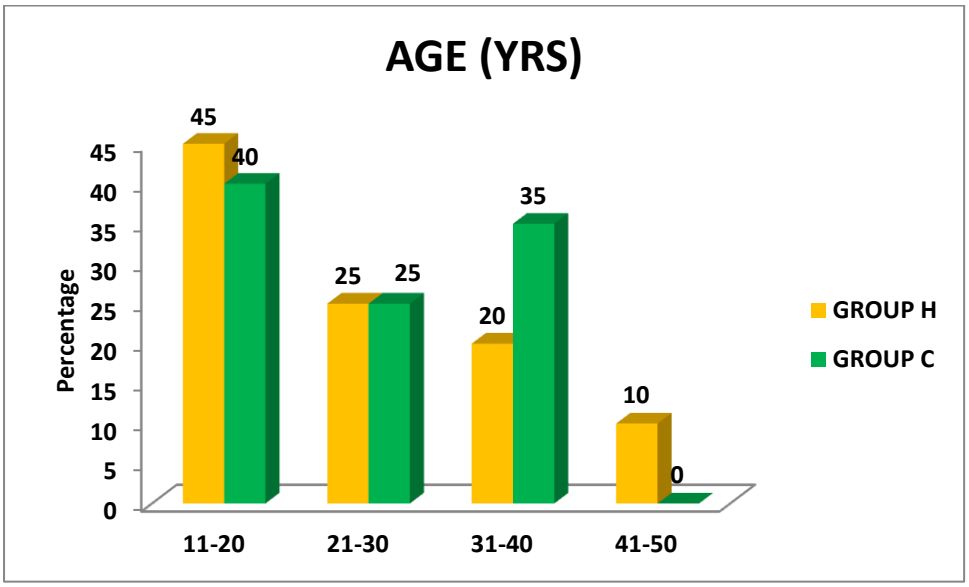


TABLE 10: MEAN AGE BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS

% OF BURNS	AGE(YRS)				p value
	GROUP H		GROUP C		
	Mean	SD	Mean	SD	
5-10	29.7	14.4	37.7	6.7	0.397
10-20	23.9	9.3	27.8	10.0	0.499
20-30	47.5	3.5	26.8	7.7	0.017*
30-40	30.3	10.5	32.1	9.1	0.761

Note: *means significant at 5% level of significance ($p<0.05$)

GRAPH 6: MEAN AGE BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS

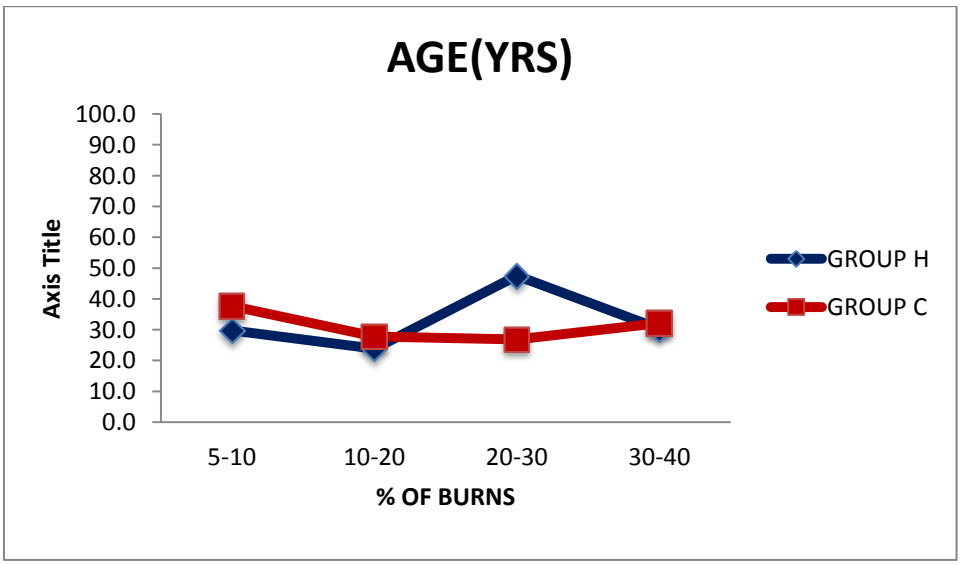
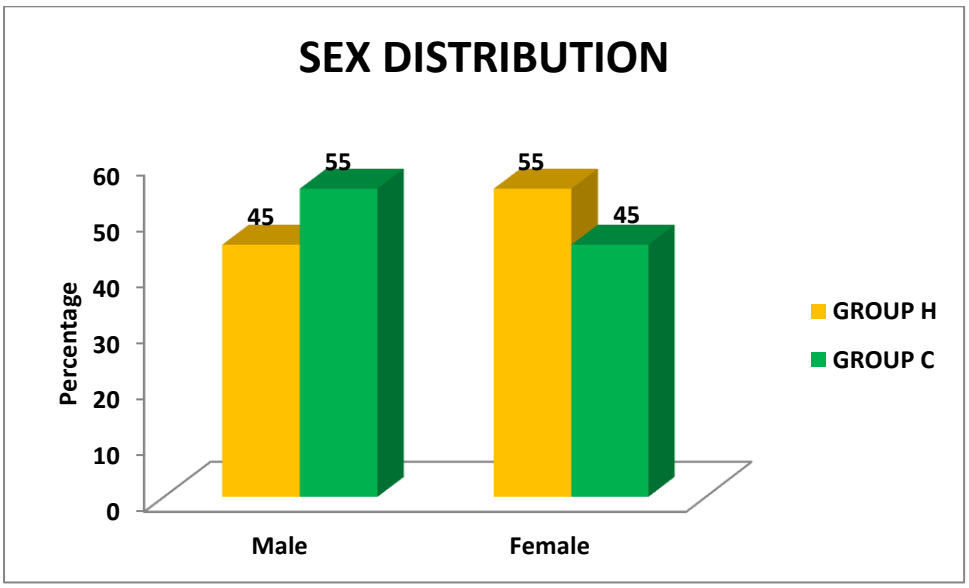


TABLE 11: DISTRIBUTION OF CASES ACCORDING TO SEX BETWEEN STUDY GROUPS

SEX	GROUP H		GROUP C		p value
	N	%	N	%	
Male	9	45.0	11	55.0	0.527
Female	11	55.0	9	45.0	
Total	20	100.0	20	100.0	

GRAPH 7: DISTRIBUTION OF CASES ACCORDING TO SEX BETWEEN STUDY GROUPS

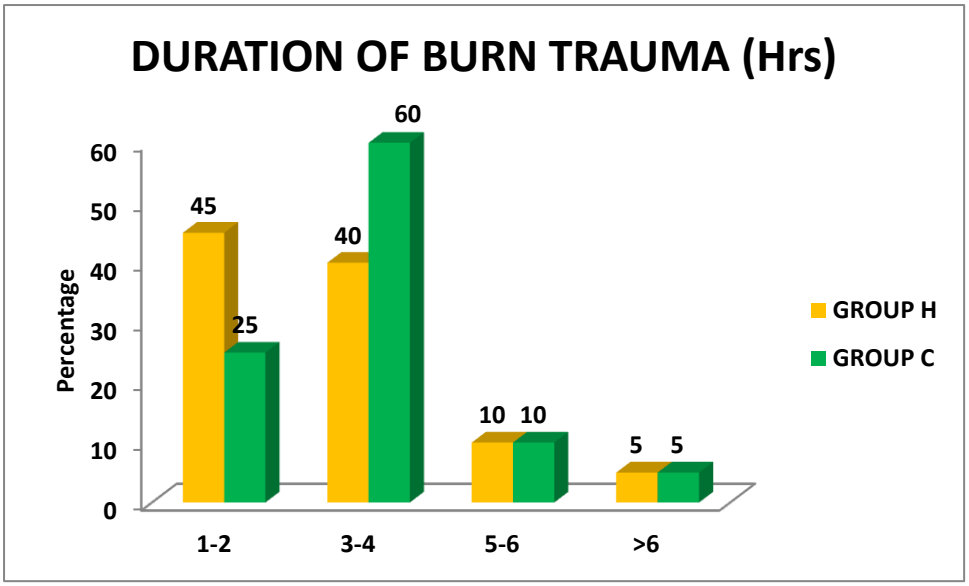


Male and female patients were almost equally distributed among both groups wherein there were 11 Males: 9 Females in Control group (55%:45%) when compared to 9 Males: 11 Females (45%:55%) in Heparin Group.

TABLE 12: DISTRIBUTION OF CASES ACCORDING TO DURATION OF BURN TRAUMA BETWEEN STUDY GROUPS

DURATION OF BURN TRAUMA (Hrs)	GROUP H		GROUP C		p value
	N	%	N	%	
1-2	9	45.0	5	25.0	0.584
3-4	8	40.0	12	60.0	
5-6	2	10.0	2	10.0	
>6	1	5.0	1	5.0	
Total	20	100.0	20	100.0	

GRAPH 8: DISTRIBUTION OF CASES ACCORDING TO DURATION OF BURN TRAUMA BETWEEN STUDY GROUPS



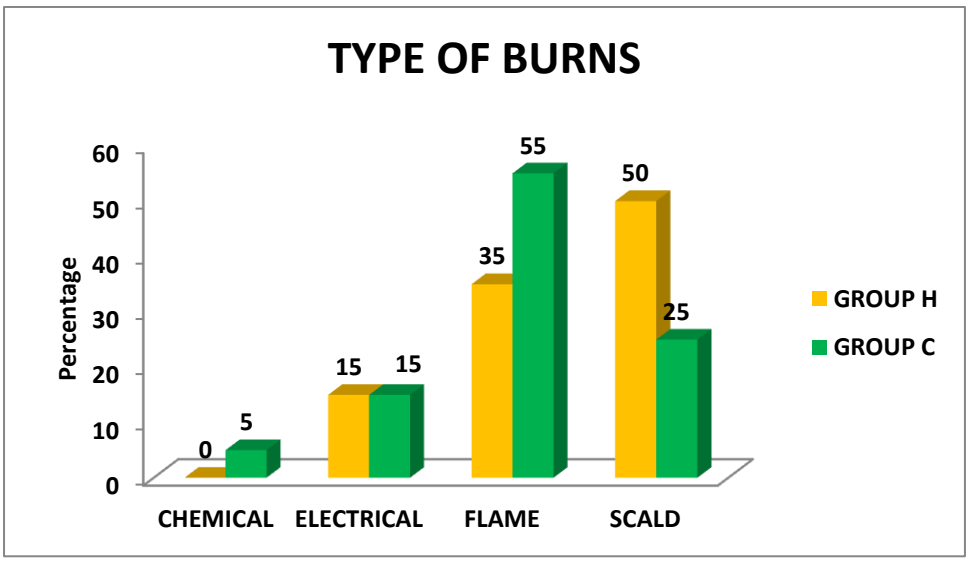
Most of our patients reported to the hospital within 4 hours of burn trauma i.e. 34 patients (85%). 4 Patients reported within 5-6 hours. 2 patients (5%) however reported post 6 hours due to our hospital being the only burn trauma care centre from their village which was about 100-150km away.

Types of Burns:

TABLE 13: DISTRIBUTION OF CASES ACCORDING TO TYPE OF BURNS BETWEEN STUDY GROUPS

TYPE OF BURNS	GROUP H		GROUP C		p value
	N	%	N	%	
CHEMICAL	0	0.0	1	5.0	0.314
ELECTRICAL	3	15.0	3	15.0	
FLAME	7	35.0	11	55.0	
SCALD	10	50.0	5	25.0	
Total	20	100.0	20	100.0	

GRAPH 9: DISTRIBUTION OF CASES ACCORDING TO TYPE OF BURNS BETWEEN STUDY GROUPS



The majority of our patients had Flame (17 patients, 42.5%) and Scald (15 patients, 37.5%) burns. 6 patients (15%) had suffered Electric Burns and the one patient had a Chemical Burn.

Pain Scores:

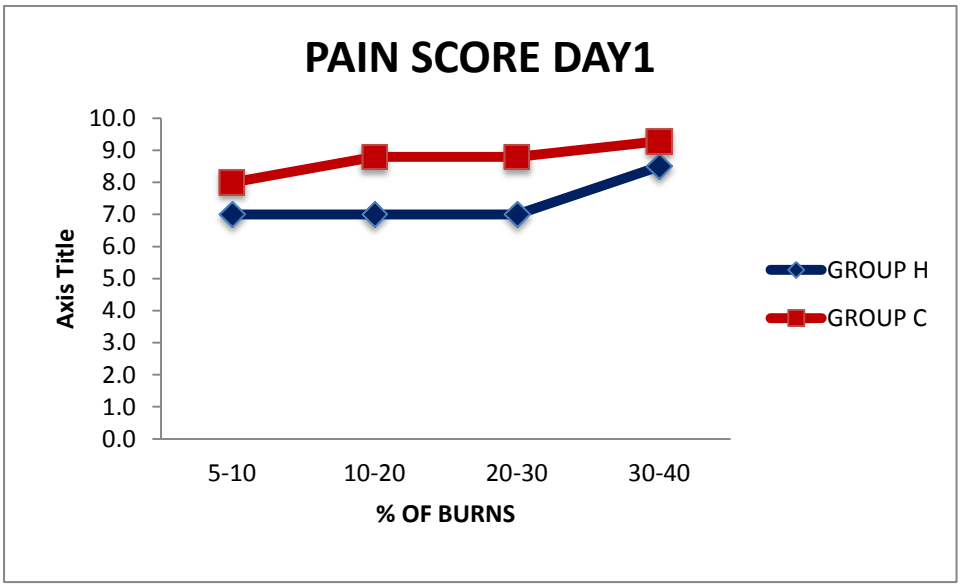
Pain Score Day 1:

TABLE 14: MEAN PAIN SCORE DAY1 BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS

% OF BURNS	PAIN SCORE DAY1				p value
	GROUP H		GROUP C		
	Mean	SD	Mean	SD	
5-10	7.0	1.7	8.0	0.0	0.362
10-20	7.0	1.0	8.8	0.4	0.004*
20-30	7.0	1.4	8.8	0.8	0.080
30-40	8.5	1.0	9.3	0.8	0.172

Note: *means significant at 5% level of significance ($p<0.05$)

GRAPH 10: MEAN PAIN SCORE DAY1 BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS



The Pain score on Day 1 was compared after administering the dose of heparin a single time for the Heparin group and cleansing the wound with normal saline for the patients in Control group.

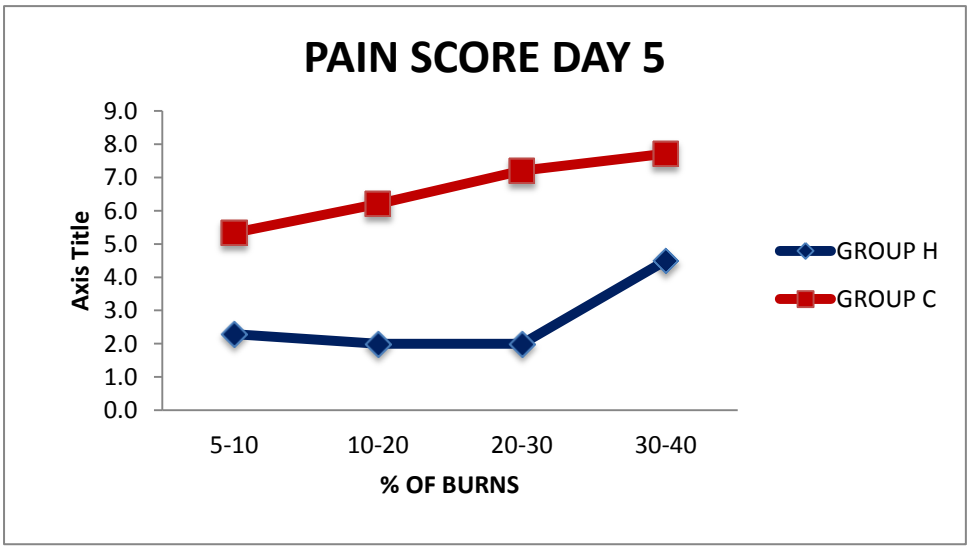
Pain Score Day 5:

TABLE 15: MEAN PAIN SCORE DAY5 BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS

% OF BURNS	PAIN SCORE DAY 5				p value
	GROUP H		GROUP C		
	Mean	SD	Mean	SD	
5-10	2.3	1.4	5.3	1.2	0.010*
11-20	2.0	0.0	6.2	1.3	<0.001*
21-30	2.0	0.0	7.2	1.1	<0.001*
31-40	4.5	1.0	7.7	0.5	<0.001*

Note: *means significant at 5% level of significance (p<0.05)

GRAPH 11: MEAN PAIN SCORE DAY5 BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS



The Pain Score on day 5 was taken after the final dose of Topical Heparin administration for the Heparin group and after removing the paraffin gauze dressing for the patients in Control group. As our results indicate, the patients in Heparin group had a significant decrease in their pain score (p value <0.001) when compared to the Control group. This concludes that heparin acted as an analgesic on topical application along with its other properties.

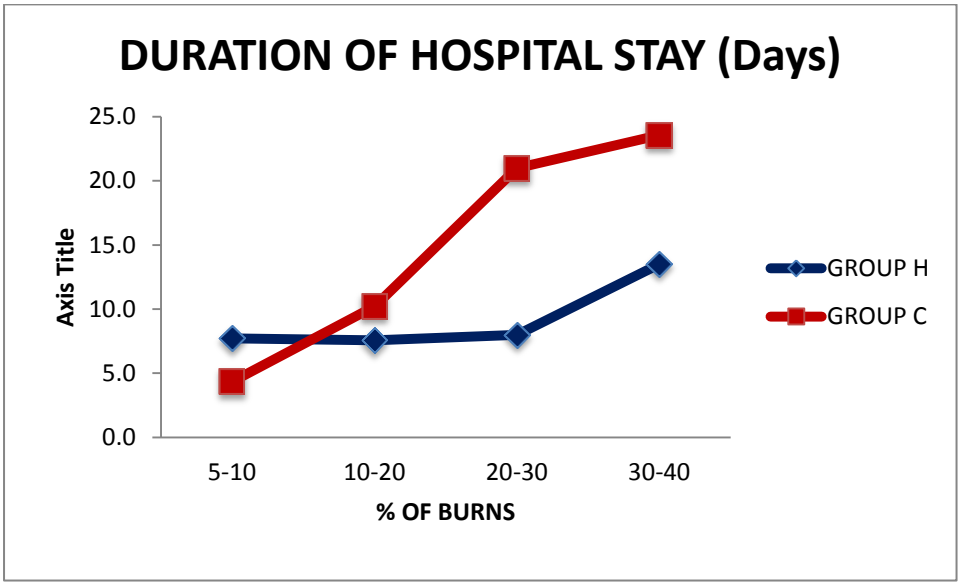
Duration of Hospital Stay:

TABLE 16: MEAN DURATION OF HOSPITAL STAY BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS

% OF BURNS	DURATION OF HOSPITAL STAY (Days)				p value
	GROUP H		GROUP C		
	Mean	SD	Mean	SD	
5-10	7.7	1.0	4.3	3.1	0.022*
10-20	7.6	0.8	10.2	2.9	0.041*
20-30	8.0	0.0	21.0	10.7	0.166
30-40	13.5	11.3	23.6	3.4	0.049*

Note: *means significant at 5% level of significance ($p<0.05$)

GRAPH 12: MEAN DURATION OF HOSPITAL STAY BETWEEN STUDY GROUPS ACCORDING TO % OF BURNS



The days of hospitalization was reduced significantly in patients receiving topical Heparin therapy when compared with the Control group. Most of the patients in heparin group were discharged in the 2nd week (i.e. 8 days) whereas most of the patients in Control group were discharged in the 3rd week. The p values suggest the same results.

Table 17: Analgesic Requirement

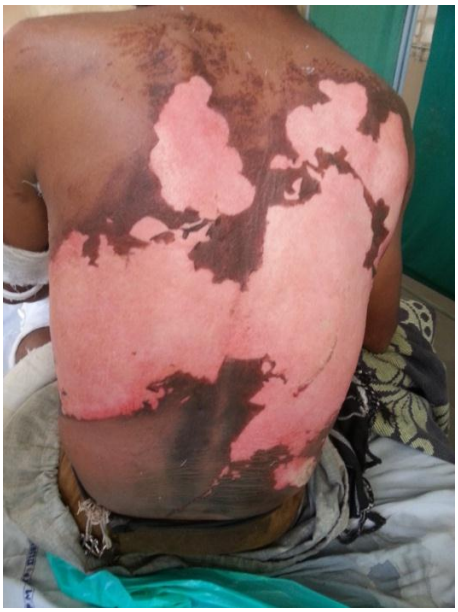
Analgesic Dosage	Group H	Group C	Total	(%)
1-2	18	7	25 patients	62.5%
3-4	2	13	15 patients	37.5%
Total	20	20	40 Patients	100%

Majority of the patients in the Heparin group (18 patients, 90%) had only 1-2 doses of analgesic medication administered to them. The Patients in Control group (13 patients, 65%) had to be given 3-4 divided doses of analgesia. This is significant as Heparin acts as an analgesic too. All these were calculated using Fishers exact test.

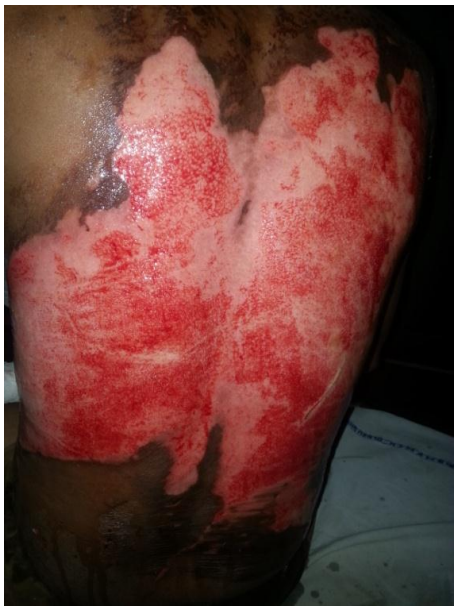
There were no complications seen in any of our patients except one wherein she had urinary tract infection on day 5 and she belonged to Heparin group.

There were no mortalities in our study.

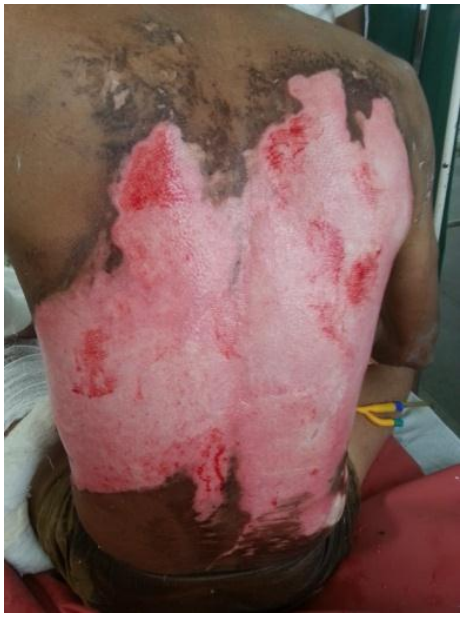
Figure 05: Heparin Group (H)



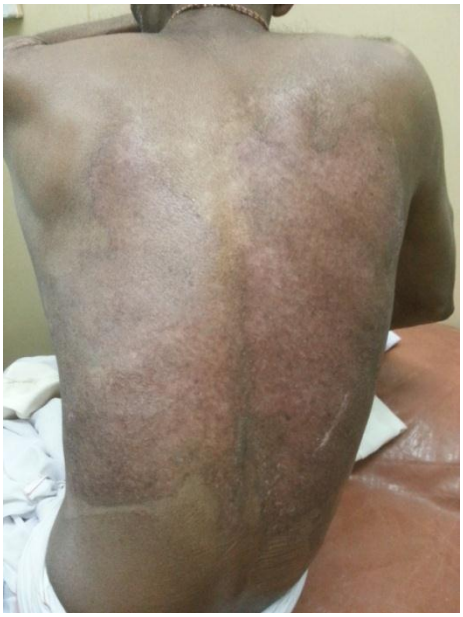
Day 1



Day 3



Day 5



Day 40

Figure 06: Control Group (C)

Day 1

Day 3

Day 5

Day 40

DISCUSSION

Burn trauma represents a major cause of morbidity and mortality, as well as a significant drain on limited health resources. The breached skin barrier is the hallmark of thermal injury. Thermal injuries produce coagulative necrosis of the skin and underlying tissues which is very painful and is associated with complex local and systemic pathology and a high morbidity and mortality. Superficial burns i.e. first degree burns heal in 5-7 days time without any scarring, while superficial dermal or deep dermal burns i.e. 2nd degree burns take anytime between 2 to 4 weeks to heal and are extremely painful.

Regardless of the technological advancements and innovative steps taken towards treatment of burns and clear understanding of the patho-physiology of burns, with the advent of good spectrum of antibiotics to prevent infection in Burns, the 2nd to 3rd degree burns are still a challenge to the surgeons in terms of management. To decrease morbidity & mortality tangential/primary excision & grafting has become imperative in 2nd to 3rd degree burns. But the efforts to prevent the progression of depth of burns, the relief of pain, the requirement of high quantities of intra-venous fluid for resuscitation & use of multiple antibiotic is still a herculean task for the surgeon.

Heparin has shown to be very effective in the treatment of burns. A number of studies on burn patients have unearthed the effects of heparin which were anti-inflammatory, neoangiogenic, reduction of tissue edema, anti serotonin and epithelializing, in addition to anticoagulation. Use of heparin in burns patients according to a protocol, maintained blood circulation, inhibited blood clotting and infarctions, relieved pain, limited inflammation, revascularized ischemic tissue,

enhanced granulation and resulted in new skin that was smooth and comfortable with minimum or no scars.

Blood and wound swab cultures were not significantly different in the two groups. There was also no significant disparity vis-à-vis the organisms isolated and their respective drug sensitivity. Analgesics, Intravenous resuscitation fluids, supportive treatment and burn care costs were much reduced. No serious complications were encountered. The addition of heparin affordably improved burn care.

During the study period from October 2015 – May 2018 a total 40 patients (who met the required criteria) with burns were admitted in the Department of General Surgery, BLDEU Shri B M Patil Medical College Hospital, Vijayapur. The patients in the study had the same parameters and characteristics, were limited to an age group of >15 years old and < 50 years old, with a variety of burn trauma (scalds, flame, electrical & chemical) of greater than 5% to less than 40% TBSA size. These 40 patients with these parameters were prospectively randomized without bias into two similar 20 patient cohort groups, a control Group labeled C, and a test-variable Group labeled H.

Requirement of Analgesia

The observation that we made in our study was that the heparin group of patients were receiving analgesics only once or twice a day for 1 week and from the start of 2nd week it was only on demand basis and very few patients opted for it. This was in contrast to the patients in control group wherein they received analgesics thrice or more in a day in the first week and in the 2nd week it was down to once or twice a day. These findings were consistent with similar observation made in a study

conducted by Agbenorku *et al* [47] who found heparin to be effective in alleviation of pain. Similar study conducted by Muhsin *et al* [44]concluded that application of heparin topically over the burn area in patients with superficial second degree burns reduced the pain significantly when compared to the conventional treatment.

Thus, in this study, anti-inflammatory effects were evident for Heparin, similar to those reported in previous studies. Initial burn erythema, when present, blanched. There was less burn site and body swelling. The relief of pain with Heparin use was remarkable. An assumption was that heparin's anti-inflammatory effects were dose related and dose dependent. This assumption was supported by the finding in this study that there was a direct relationship between increasing size of burns of similar severity and increasing amount of heparin required to produce an equal degree of healing. The reduced use of pain medication and reduced side-effects from pain medicine permitted Heparin Group patients, who were more alert and cheerful, to more easily breathe, eat, move, and participate in their burn treatment, compared to Control Group patients. The overall quantity of analgesics used and the frequency of administration were less in Heparin Group. Statistical analysis on the basis of Fishers exact test showed a very high significance in the reduction of need of analgesics by patients in Heparin Group than the Control Group.

Duration of Hospital Stay

Majority of the patients in the heparin group had a hospital stay of 8 days, whereas most of the patients in the control group were discharged in the 3rd week (p value <0.05). Studies conducted by Agbenorku *et al* [47]& Muhsin *et al*[44] have reported that the patients treated with heparin spent less time in the hospital and were discharged early. The patients in heparin group had an improved outcome when

compared with the patients in control group with respect to reduced pain, reduced tissue edema and restriction of burn wound spread which all translated into reduced duration in their hospital stay.

The acceptable appearance of the new skin was generally better in Heparin Group compared to Control Group patients in this study. In our part of the world with most of our patients belonging to lower socioeconomic group, a reduced stay in the hospital meant a quick return to work. The mean duration of hospital stay was significantly less in the Heparin Group compared the Control Group. The shorter stay increased the cost effectiveness, decreased mental and economic hardship faced by the patient and the patient's family due to loss of man hours. Not only does it quickly rehabilitate the patient in the society, but it also has advantages for hospital administration in the form of reduced bed occupancy thus making the beds available to other patients in need.

Wound Healing

We are happy to state that in our study we have not encountered any complication regarding wound healing or otherwise. There was only one side effect in one patient being treated with topical heparin application (the patient developed urinary tract infection). Apart from this there were no morbidities. Our observation is strikingly similar to one study conducted by Venkatachalapathy *et al* [34] wherein patients treated with heparin solution had fewer complications and side effects.

There were benefits to doctors and nurses and ancillary therapists with heparin use. In Heparin Group patients, the benefits of relieved pain, along with the fewer water baths and dressings, and no use of time consuming antibiotic topical creams application, rendered the treatment of Heparin Group patients more pleasant and

easier than in Control Group patients. The Burn Unit ambience was notably quieter, calmer and more pleasant as well.

With heparin use the burn blisters, which were not removed and which rarely became infected, functioned as natural skin grafts which required no further care. The revascularization of ischemic tissue, and the improved quality and greater quantity of vascular granulation tissue were noteworthy, consistent with earlier post-burn features with Heparin use in Heparin Group patients. These improvements were presumed to be a function of heparin, as research found neoangiogenic effects reported in Heparin use in burn and non-burn studies. With the use of heparin, capillary endothelial cells were stimulated to migrate into ischemic tissues where they multiplied and formed new capillary blood vessel systems that on perfusion with blood restored blood flow into the ischemic tissues.

Clinically noted, without determination of quantity, there was a reduction in burn surface infections in H patients compared to Control Group. One explanation may be that orally administered antibiotics were able to reach the burns from within the body via the increase in blood flow mediated by the enhanced neoangiogenic-revascularization of the ischemic burns which was consistently evident in Heparin Group patients compared to Control Group, which was similarly reported in previous studies. A reduction in intestinal bacterial translocation and sepsis found in a research study may be another partial explanation for burn infection reduction in this study. Bleeding and Clotting time was analyzed; no bleeding problems or other serious complication occurred in the Heparin Group patients in this study. The acceptable appearance of the new skin was generally better in Heparin Group compared to Control Group patients in this study. The topical use of Heparin was found to be safe in this study.

Cost Analysis

As a fortiori to the above mentioned observation, in the study that we conducted, we calculated the average cost and expenditure on the intravenous antibiotics and made a comparison between the two study groups and we found that the patients treated with heparin had to spend an average of Rs.910 per day whereas the control group had to shell out an additional Rs. 300 on what the Heparin group was already paying. Similar cost benefits were reported in studies conducted by Muhsin *et al* [44] and Venkatachalapathy *et al* [34].

A thorough study conducted in our hospital clearly suggested that Heparin as a topically administered agent for burns and burn trauma significantly improved the general condition of the patient, provided adequate analgesia, decreased the spread of burn surface area, reduced complications and decreased the overall cost by reducing the hospital stay and making sure that the patients returned to their economically productive life at a faster pace when compared to the patients in the study group. Hence Heparin treatment, which in addition to providing medical benefits, if cost effective, will be readily acceptable by healthcare providers and patients the world over.

Limitations of this study

Over the past three years, we have studied a total of 40 patients fitting the above mentioned criteria and would recommend a larger study group in future studies on this topic with a few other parameters not included in ours. We restricted our study to a burn percentage of 40% only; study of higher burn percentage patients is required and should be done.

CONCLUSION

Unfractioned Heparin which was used in our study had the following conclusion

1. In similarly treated equal number of statistically similar patients with similar burns, the addition of heparin administered topically in the initial week significantly reduced the total duration of hospitalization.
2. Patients who received heparin had better relief of pain with lesser requirement of parenteral opioids.
3. The time for healing and the quality of skin (post treatment) was superior in patients who received heparin.
4. The lack of burn wound extension in heparin group was clearly noticeable.
5. There was one complication (i.e. UTI) in Heparin group.
6. The average cost of patients treated with heparin was significantly lesser than its counterpart. Hence it is cost effective.
7. There were no mortalities in either group.

SUMMARY

A total of 40 patients were selected based on the inclusion and exclusion criteria, and divided into equal cohorts of 20 each which were statistically similar. In addition to the standard treatment protocol the test group received topical aqueous heparin solution and control group received topical antimicrobials. Both groups were analyzed for relief of pain (i.e. their analgesic capabilities), reduction in tissue edema, absence of infection, revascularization, and appearance of granulation & re-epithelization of deeply burned tissue. The results were compared using Student‘t’ test, Chi square test, Paired ‘t’ test and Fishers exact test. There was a statistically significant ($p < 0.001$) difference in the analgesic needs in heparin and control group. From the study it was concluded that heparin applied topically reduced pain, duration of hospital stay, had lesser complications and had lesser rates of wound infection.

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ANNEXURE I

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

NO/58/2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17-11-2015 *at* 03 pm *scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.*

Title "Role of heparin in the Management of Burns"

Name of P.G. Student : Dr Ritesh. G.V.
Dept of Surgery

Name of Guide/Co-investigator : Dr Aravind V Patil
Professor.

DR.TEJASWINI VALLABHA
CHAIRMAN

Following documents were placed before E.C. for Scrutinization
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

SAMPLE INFORMED CONSENT FORM:

TITLE OF THE PROJECT : **ROLE OF HEPARIN IN THE MANAGEMENT OF BURNS**

PG GUIDE : **DR. ARAVIND V PATIL**
M.S. (GENERAL SURGERY)
PROFESSOR OF SURGERY
DEPARTMENT OF SURGERY

PRINCIPAL INVESTIGATOR : **DR.RITESH GV**

PURPOSE OF RESEARCH:

I have been informed that this study is conducted to prove the effectiveness of topical Heparin administration with that of Conventional treatment in the management of burns.

PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

Patients who met the inclusion criteria were randomly assigned a control group (Group C) or heparin group (Group H). 20 patients were started on topical heparin (Group H), while the other 20 patients in the control group (Group C) were treated with conventional dressings with silver sulfadiazine, intravenous antibiotics, analgesics and intravenous fluids.

The dose of heparin required for topical application was calculated to be 100,000 IU/15% burn surface area (BSA) per day in 3-4 divided doses. The medication was applied to the burnt surface drop by drop with a 20 mL syringe, until the pain was relieved, repeated for 2-4 times until blanching occurred. Beginning on the 2nd day, heparin was applied twice a day, using a diminishing quantity for 1 week.

Blisters were rinsed with heparin solution with a hypodermic needle and were not de- roofed.

Relief of pain as recorded by a visual analog scale (VAS) & Wong-Baker faces scale healing of wounds, complications, mortality and duration of hospital stay were reported and analyzed.

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the examination or during my treatment. This is mainly the result of my condition and the procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in the study will help to predict the efficacy of topical heparin therapy against conventional treatment modality in the management of burns.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study to **Dr. Ritesh GV** in the Department of General Surgery who will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Ritesh GV may terminate my participation in the study after he has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me. But, no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. Ritesh GV
(Investigator)

Date

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Ritesh GV has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to signature) Date

PROFORMA FOR CASE TAKING

SL NO

Name

Age IP NO

Sex UNIT

Religion DOA

Occupation DOD

Address:

Mobile No:

Duration of Burn Trauma:

Type of Burns: Flame/Scald/ Chemical/ Electrical

Cause of Burns: Accidental/ Suicidal/ Homicidal

Associated Co-morbidities (if any):

HISTORY OF PRESENT ILLNESS:

PERSONAL HISTORY:

GENERAL PHYSICAL EXAMINATION:

Built: Well/Moderate/Poor

Nourishment: Well/Moderate/Poor

Temperature: Pulse: SPO2:

Blood Pressure: Respiratory Rate:

SYSTEMIC EXAMINATION:

Per Abdomen

Respiratory System

Cardio Vascular System

Central Nervous System

LABORATORY TESTS

Haemoglobin% :

Total Count :

Platelets :

Differential Count

Neutrophil :

Lymphocytes :

Eosinophils :

Basophils :

Monocytes :

Blood Urea :

Serum Creatinine :

Serum Albumin :

Serum Electrolytes : Na+ K+ Ca+ Cl-

APTT :

PT/ INR :

HIV :

HBsAg :

BT/ CT :

Electro Cardiogram :

Ultrasonography of Abdomen:

Chest X-ray : (as and when necessary)

OTHERS :

Percentage of Burns:

Depth of Burns:

Patient Treatment Plan – Conventional / Topical Heparin

Heparin started on:

Heparin stopped on:

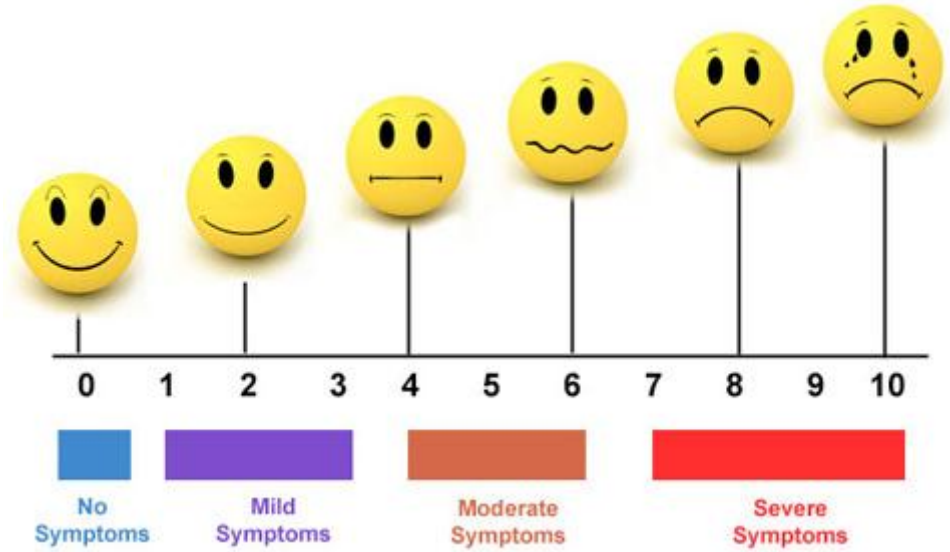
DIAGNOSIS:

RESULTS FOR PAIN GRADING ACCORDING TO WONG – BAKER FACES

DAY	0	1	2	3	4	5
CONVENTIONAL THERAPY						
POST- HEPARIN APPLICATION						

FINAL DIAGNOSIS :

Follow up :



KEY TO MASTER CHART

M = Male

F = Female

H = Heparin

C = Control